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DYSENTERY-LIKE DISEASES (PARADYSENTERY, PARATYPHOID) IN CHILDREN AND THEIR CAUSES

ONE PLATE

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Bloody or purulent stools mixed with mucus are more commonly observed in children than in adults. The condition may be relieved in a few days or may by degrees increase in intensity until grave symptoms of intoxication ensue and in some cases severe fulminating symptoms develop with death on the second or third day. During the past 9 years I have studied in our clinic several hundred such cases, from 334 of which the 5 kinds of ordinary dysentery bacilli have been isolated, while in 73 organisms have been obtained which belong apparently to a hitherto undescribed species.* From a few of the cases I obtained cultures of Bacillus paratyphosus and a bacillus allied to the paratyphoid group. I have also cultivated Morgan's [1] bacillus, and a variety similar to the strains isolated by Leiner,[4] although I could not confirm their claims that they bear any relation to the clinical condition. This paper is a report on those organisms which I believe are new. Those that resemble ordinary dysentery bacilli I shall speak of as paradysentery bacilli, and those that resemble paratyphoid bacilli as paratyphoid-x bacilli. The reason for these terminologies will be evident later.

PARADYSENTERY GROUP

In the early stages of the disease the organism may be isolated almost in pure culture, but in most cases it is associated with the colon bacillus. As the disease progresses its isolation becomes more difficult.

Several different strains have been obtained which may be divided into two kinds, according to their behavior toward carbohydrates, having common characteristics otherwise.

The form of the colonies in the agar plate is somewhat larger than that of the true dysentery bacillus. Moreover, besides the regularly formed colonies, such as are seen in cultures of dysentery bacilli, this organism forms also thinner, somewhat larger colonies, a trifle elevated in the center, with quite irregular edges and sometimes with

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Received for publication July 16, 1921.

* Of 7 cases of dysentery in children examined in Chicago in the summer of 1921, 4 yielded the Hiss' bacillus, 1 the Shega bacillus and in 2 the cultures proved negative.

[1] Brit. Med. Jour., 1907, 2, p. 15.

a kind of lobular outline as if undergoing disintegration. When first isolated from the feces, the colonies are usually irregular. This is one of the characteristics by which this group can be differentiated from the true dysentery group.

Morphology.—The size is about the same as that of the colon bacillus, and the organisms usually occur singly, although long chains are sometimes seen extending throughout half the field. The organism stains well with anilin dyes, intensely at the ends and less so in the middle. There are no flagella.

Motility.—The organisms have no proper motility, although they have molecular movement.

Biologic Characteristics.—In a gelatin stab growth is obtained along the stab line, but there is no liquefaction.

Abundant growth is obtained around the stab canal in glucose agar, but there is no gas production.

Good growth is obtained in 1 to 2% Witte peptone solution, and there is no scum formation after continuous prolonged cultivation. There is a more distinct sedimentation of the organisms, than in the case of the dysentery bacilli.

No indol has been demonstrated, even in 1 to 2% Witte peptone solution.

New, freshly isolated strains coagulate milk after from 2 to 3 weeks' cultivation; older cultures after repeated subcultures showed coagulin in 10 to 14 days. Coagulation begins at the bottom and gradually progresses throughout the upper layer. It is complete in 3 to 7 days, when the clear solution is separated out.

Litmus whey is turned red in 24 hours, violet in 3 to 5 days, and red again within the next 2 to 4 days; or it may be violet or red within 24 hours, then blue and finally once more violet or red.

Litmus nutrose glucose solution develops acid and red color, with coagulation after 24 hours.

Carbohydrate decomposition was studied in a solution containing mannite, etc., in a proportion of 1.3% to 1% Witte peptone solution, to which litmus was added as indicator. Mannite and dextrose were split into acid after one day.

Dextrin and maltose were split by both varieties of paradysentery bacilli, but the first type renders these sugars acid the following day, while the second type changes the color after 1-2 weeks; that is, within several days the color changes into violet and after a longer time turns into red. In general, maltose is somewhat more quickly decomposed than dextrin.

Saccharose and lactose are slowly decomposed by both groups, requiring 2 to 3 weeks; the color first becomes violet, finally red.

Comparison of the carbohydrate reactions only of the paradysentery and the true dysentery bacilli shows the first type of the former group to be apparently indistinguishable from the type 4 (Flexner) and the second from type 2 (Y), but the paradysentery bacillus when kept in culture for many weeks behaves, as has been stated, like the colon bacillus. I have therefore divided the paradysentery strain into 2 types: A, which decomposes maltose and dextrin within 24 hours, and B, which causes no change whatever for several days.

Differentiation of These Two Varieties of Bacilli from Other Familiar or Similar Organisms.—Differentiation from similar organisms, such as typhoid, paratyphoid, and other motile bacilli is very simple. Among the colon varieties there is one which decomposes dextrose into acid but forms no gas, and after a few days coagulates milk, but this can be differentiated from our organisms by the time required for the coagulation of milk or the splitting of the carbohydrate, through the forms of colony, and also by means of agglutination reactions. The differentiation from the dysentery bacillus is made by means of agglutination reaction with immune serum, the form of colonies, and by the coagulation of milk. It is true that in the literature there are a number of bacilli isolated from patients with dysentery-like symptoms that resemble ours, for example, those of Duval,[2] Torrey[3] and Leiner,[4] but while the organism described by Duval resembles ours with respect to the behavior on lactose, Duval's bacillus did not coagulate litmus milk and agglutination placed it in the typhus group while my paradysentery bacilli coagulate milk and differ in agglutination from the typhoid group. Torrey's bacillus C also did not coagulate litmus milk, although his older strains sometimes showed coagulation. But to exactly differentiate varieties of similar bacilli requires comparative methods. Leiner's bacillus resembles my strains in its coagulation of milk and carbohydrate reactions, but the colonies are knobbed and agglutination places it among the saprophytic colon bacilli. It appears, therefore, that the organisms in question represent an independent, specific, pathogenic bacterium.

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[2] Jour. Am. Med. Assn., 1904, 43, p. 381.

[3] Jour. of Exp. Med., 1905, 7, p. 385.

[4] Centralbl. f. Bakteriol., I, O., 1907, 43, p. 783.

In 56 of the 73 cases from which the paradysentery bacillus was isolated type A was obtained, in 17 type B. Although type B was so seldom found, it is an interesting strain, as shown by comparison of the carbohydrate reactions of the 2 types with those of the dysentery bacillus, type A resembling type 4 of dysentery bacillus (Flexner), and type B resembling type 2 of dysentery bacillus (Y).

IMMUNOLOGIC RELATIONS

Agglutination.—The strains which I isolated were agglutinated by the serum of the patients from which they were obtained in dilutions of 300:500 and not infrequently 1,000, but were not agglutinated by the serums of other patients or normal persons. The agglutination titer was in general greater than that usually shown by the dysentery serums for dysentery strains. The 2 types of paradysentery bacillus were affected in practically the same way by the patients' serums, hence they cannot be differentiated from each other by agglutination reactions, although their biologic properties are different. The same holds true of the dysentery bacilli of lower classes, such as 4 or 5 types, the types of which cannot be differentiated by agglutination reactions. Strains of the paradysentery bacillus which have been maintained by cultivation for a long time have the property of auto-agglutination, a phenomenon observed among other pathogenic bacteria.

Complement fixation.—The extract of both types of the paradysentery bacillus fixes complement in the presence of homologous serum.

Virulence for Animals.—The paradysentery bacillus, whether living or killed, is virulent for all ordinary laboratory animals when injected intraperitoneally or into a vein (1-2 slant agar culture for young rabbits, 3-5 mg. for guinea-pigs, and 0.2-1 mg. for mice), but the virulence is not strong nor definite. Sections of the animal tissue showed no significant changes in the intestinal wall. In this respect the organism is analogous to the so-called acid dysentery bacilli.

CLINICAL

Of the 73 children from whom the paradysentery bacillus was isolated, the youngest was 9 months old and the oldest 13 years; I have also seen two adult cases. The disease was prevalent at all times, but was most frequent in the summer months.

Symptoms and Course.—The disease caused by the paradysentery bacillus is difficult to differentiate clinically from that caused by the true dysentery bacillus, except that in the case of the former the intestinal symptoms, as well as the general symptoms, are milder than in the latter, and recovery follows as a rule within a few days.

At onset the fever is about 38-39 C., not infrequently higher, the stools are bloody and mixed with mucus and pus; on the day of onset or the following day there may be 10 stools or so, but on the 2nd or 3rd day the temperature falls and stools are less frequent; 2-3 days later there are only 2 or 3 stools. In most cases in 7-10 days the stool is almost normal or the patient may even be constipated. On palpation of the abdomen one sometimes feels, as in dysentery, cord-like thickening, but this is often absent. Tenesmus is also usually insignificant, because the intestinal inflammation is mild in character.

The symptoms just described are those seen in the greater number of cases, but in more than 15% of all cases on the day of onset there are severe symptoms of intoxication, that is, high fever, drowsiness, cramps, coma, vomiting, weak and frequent pulse, coffee grounds hemorrhagic vomit, marked acetonuria, etc., and most of these become fulminant and end fatally in 2-3 days after onset. Cases are known in which patients, who on the day of onset have shown no special symptoms of intoxication, on the 3rd or 4th day show signs of severe intoxication (vomiting, heart weakness, frequent pulse, coffee ground vomit, jactitation, etc.) and in a few days they die. The latter form is less frequent than the fulminating. The fulminating symptoms of all these cases resemble those of the bacillary dysentery in children. But in paradysentery, the disappearance of the intoxication is followed by rapid convalescence, for the intestinal symptoms are less severe than in true dysentery.

Infectivity.—Members of the same family may become ill simultaneously, or at an interval of a few days. It happened that a mother nursing her child became infected with the same type of organism, thus demonstrating that these organisms possess infectivity, similar to other pathogenic bacteria.

Anatomic Changes in the Intestinal Wall.—Since 1913, when this group of bacilli was first demonstrated, I have made 6 postmortem examinations—3 persons who died within 36 to 60 hours after the onset of illness, and 2 on patients dying on the 5th and 14th day, respectively. We may include another case in which an improvement of the dysenteric symptoms took place, but the patient died on the 23rd day from septicemia. It was possible to isolate the causative agent from the intestinal tissues in all these cases except the last.

The following changes were observed in the intestines after death with fulminating symptoms: There was swelling of the lymphatics of the small intestine, especially below the ileum—a particularly characteristic change. The mucosa itself showed no special alterations except slight edema and hyperemia, the latter being, however, more marked on the wall of the large intestine, the follicles of which were swollen and showed erosions or slight ulcers. There were indications of a desquamation of epithelial cells, and occasionally one found a fine, branny coating which microscopically was shown to consist of loosened epithelial and blood cells, etc. These changes are similar to those found in true dysentery, except that in the latter disease the inflammation of the mucosa of the large intestine is far more marked. The indication of manifest diphtheric membrane, such as occurs in true dysentery, could not be found in fulminating cases. The changes found in the small intestine did not differ from those of dysentery.

The necropsies on patients ill for more than 5 days showed the so-called diphtheric inflammation of the large intestine, although not as marked as in dysentery; the lower part of the ileum occasionally showed slight diphtheric inflammation. In short, while the changes of the intestinal mucosa in paradysentery infection resemble those of dysentery, they are slighter in degree.

The other viscera showed no marked changes except parenchymatous degeneration, hyperemia, etc. Occasionally there were a circular, duodenal ulcer, and erosions or small ulcers on the mucosa of the stomach. In fulminating cases the thymus not seldom seemed enlarged.

TERMINOLOGY AND CLASSIFICATION

As already stated, bacteriologically as well as pathologically, i. e., as indicated by the clinical phenomena and the changes of the intestinal wall, these bacilli are related to the true dysentery types, the only difference being that the changes caused by them are less severe in character than are those of true dysentery. The organisms are not, however, identical with the dysentery bacilli and for that reason I have employed the term Bacillus paradysenteriae, A and B, and called the disease caused by them, paradysentery. It is rational and practicable to separate dysentery and paradysentery according to the causative agents, as we do in the case of typhoid and paratyphoid, although the two diseases in each case have certain clinical and anatomic resemblances. In English, American and German literature the so-called acid strains of dysentery bacilli are referred to sometimes as paradysentery bacilli, but as it is desirable that all types of the dysentery bacillus which possesses in general similar biologic properties should be regarded as constituting a single group, as emphasized by Shiga in Japan,[5] Lentz in Germany,[6] and Hiss in America.[7]

COMPARISON OF DYSENTERY AND PARADYSENTERY

A comparative study of cases yielding the dysentery and paradysentery organisms observed for a 4-year period (1916-1919, inclusive), during which particular care was exercised in the isolation of the paradysentery organisms, comprises 195 cases of the former and 65 of the latter, or a ratio of 3 : 1. As already stated, the patients suffering from paradysentery in general show less marked symptoms, so that they are likely to come under our treatment less frequently than those suffering from dysentery. Hence it would seem that the ratio given is not absolutely correct and that the proportion of cases of paradysentery is probably larger than here indicated.

The children suffering from fulminating symptoms of paradysentery range in ages from 2 to 6 years, and the course of the disease is similar to that of dysentery of the fulminating type. However, such fulminating symptoms are not infrequently present after orthopedic operations for congenital malformations, such as talipes equinovarus, congenital articular paralysis, etc., and some times such fulminating symptoms develop without the presence of any kind of pathogenic organism. According to our observations, these symptoms in dysentery and paradysentery are referable to the constitutional disposition of the patient rather than to the toxic action of the bacteria.

PARATYPHOID-X BACILLUS

As already stated, the organisms isolated by the writer from cases showing dysenteric symptoms were, as a rule, B. dysenteriae and B. paradysenteriae. But in a number of cases I was able to demonstrate true paratyphoid B and the paratyphoid X bacilli (Mita). I shall now describe the general properties of the paratyphoid X bacillus.

The bacilli may be cultivated abundantly by isolating them from the mucoid stools in the early stages of the disease. Colonies grown on an agar medium are spherical and resemble those of the dysentery and paratyphoid bacilli. The bacilli, which are of the same size as B. coli, at times show threadlike connections and stain with various anilin dyes; they are gram-negative. It is difficult to say whether or not they have flagella. Although some of them seemed to me to have a feeble active motility, none has been seen to move across the field of vision. Most of them show molecular activity.

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[5] Clinical Bacteriology and Infectious Diseases (Japanese), 1914.

[6] Kolle and Wassermann, Handb. d. path. Mikroorganismen, 1914, 3, p. 905.

[7] Hiss and Zinsser, Textbook of Bacteriology, 1917, p. 435.

Indol.—Our paratyphoid bacilli do not form indol even after remaining for a long time in from 1 to 2% Witte peptone solution.

Milk.—They do not coagulate milk or cause it to separate, even after long cultivation.

Litmus Whey.—After 24 hours the bacilli stain litmus whey a fast violet, occasionally a moderate red followed by violet.

Witte Peptone Solution.—There is no scum formation after long continued cultivation in Witte peptone; the solution becomes slightly cloudy.

Gelatine Stab Cultures.—These show good growth along the line of the stabs; there is no liquefaction.

Neutral Red Glucose Agar Stabs.—These show feeble gas formation and fluorescence.

Carbohydrate Decomposition.—In 1 to 2% Witte peptone solution, containing respectively 1.3% of mannite, dextrose, saccharose, maltose, dextrin, or lactose, the mannite and dextrose were converted into acids and gases, but the other sugars failed to decompose. The bacilli differ in this reaction from paratyphoid A and B, as dysentery 2 (Y) differ from type 4 (Flexner).[8]

Differentiation.—The paratyphoid X bacilli will be agglutinated by the serum of the patients from whom they are isolated, as well as the serum of the immunized rabbits. Agglutination takes place in a dilution of 160:320.

The extract of the bacilli produces complement deviation with the patients' serum and immune rabbit serum.

Paratyphoid X bacillus isolated for the first time in 1917, and another strain possessing the same characteristics was isolated in 1919. The two strains show reciprocal agglutination and complement deviation. The serum of patients yielding the organisms failed to agglutinate other types of bacilli, nor does the serum of rabbits immunized with these bacilli agglutinate the latter. Furthermore, the X bacilli show no agglutination reaction with the serum produced by injecting other bacilli.

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[8] Kolle and Wassermann: Handbuch. d. path. Mikrcorganismen, 1914, 3, p. 1005.

TABLE 1

Differentiation of the True Dysentery, Paradysentery (Mita) and Paratyphoid Bacilli Groups

Group	Type	Motility	Liquefaction of Gelatin	Indol Production	Litmus Whey	Milk Coagulation	Fermentation of Carbohydrate						Remarks
							Mannite	Dextrose	Saccharose	Maltose	Dextrin	Lactose	
The true dysentery bacilli group	Type 1	Molecular	—	—	* later I or I later —	—	—	*	—	—	—	—	Shiga type
	Type 2	Molecular	—	+	* later I or I later —	—	*	*	—	— or — later *	—	—	Y type
	Type 3	Molecular	—	+	* later I or I later —	—	*	*	— later *	— or — later *	—	—	Strong type
	Type 4	Molecular	—	+	* later I or I later —	—	*	*	— later * or — later —	*	*	—	Flexner type
	Type 5	Molecular	—	+	* later I or I later —	—	—	*	— later — or — later *	*	*	—	
Paradysentery bacilli group according to Mita	Type A	Molecular	—	—	* later I later * or I later — later *	— later +	*	*	— later *	*	*	— later *	Like type 4†
	Type B	Molecular	—	—	* later I later * or I later — later *	— later +	*	*	— later *	— later *	— later *	— later *	Like type 2†
Paratyphoid bacilli group	Type X (Mita)	Slight motile?	—	—	* later I or I	—	+	+	—	—	—	—	Like type 2‡
	Type A	Actively motile	—	—	* later I or I	—	+	+	—	+	*	—	Like type 4‡
	Type B	Actively motile	—	—	I later —	— later clear	+	+	—	+	+	—	

† Of dysentery bacilli during beginning of fermentation.
‡ Of dysentery bacilli unless gas formation.
+ = positive, acid and gas, or coagulation of milk.
— = negative, no change, or alkaline.
* = acid, but no gas.
I = slight acid.

CLINICAL OBSERVATIONS OF PATIENTS YIELDING THE X BACILLUS

The bacilli isolated in 1917 were obtained from a child evacuating dysenteric stools containing mucus and traces of blood. The patient, a 2-year old girl, who died 2 weeks after the onset of the disease, also showed typhoid symptoms, i. e., continuous fever and the evacuation of 2 or 3 mucoid stools daily.

The same bacilli were isolated in 1919 from 2 cases, a brother 4 years old and a sister 6 years old, who were taken ill at the same time. These patients had general and intestinal symptoms not readily distinguishable from mild dysentery. The temperature was about 38 C. on the first day when there were 8 or 9 mucoid stools mixed with blood and pus, but on the following day the stools diminished to 1 or 2, and the temperature fell; after a week constipation set in. As already stated, these bacilli were isolated from only a few patients, in one case from a patient suffering from socalled typhoid symptoms, and in 2 others from patients showing symptoms resembling those of mild dysentery.

NAME AND CLASSIFICATION OF PARATYPHOID X

While the organisms were isolated from patients showing dysenteric symptoms and also those showing typhoid symptoms, in their characteristic of changing mannite and dextrose into acids and gases, they were analogous to the paratyphoid group. For the reasons cited, I have classed the bacilli in question with the paratyphoid group, and have named them "paratyphoid X bacilli."

SUMMARY

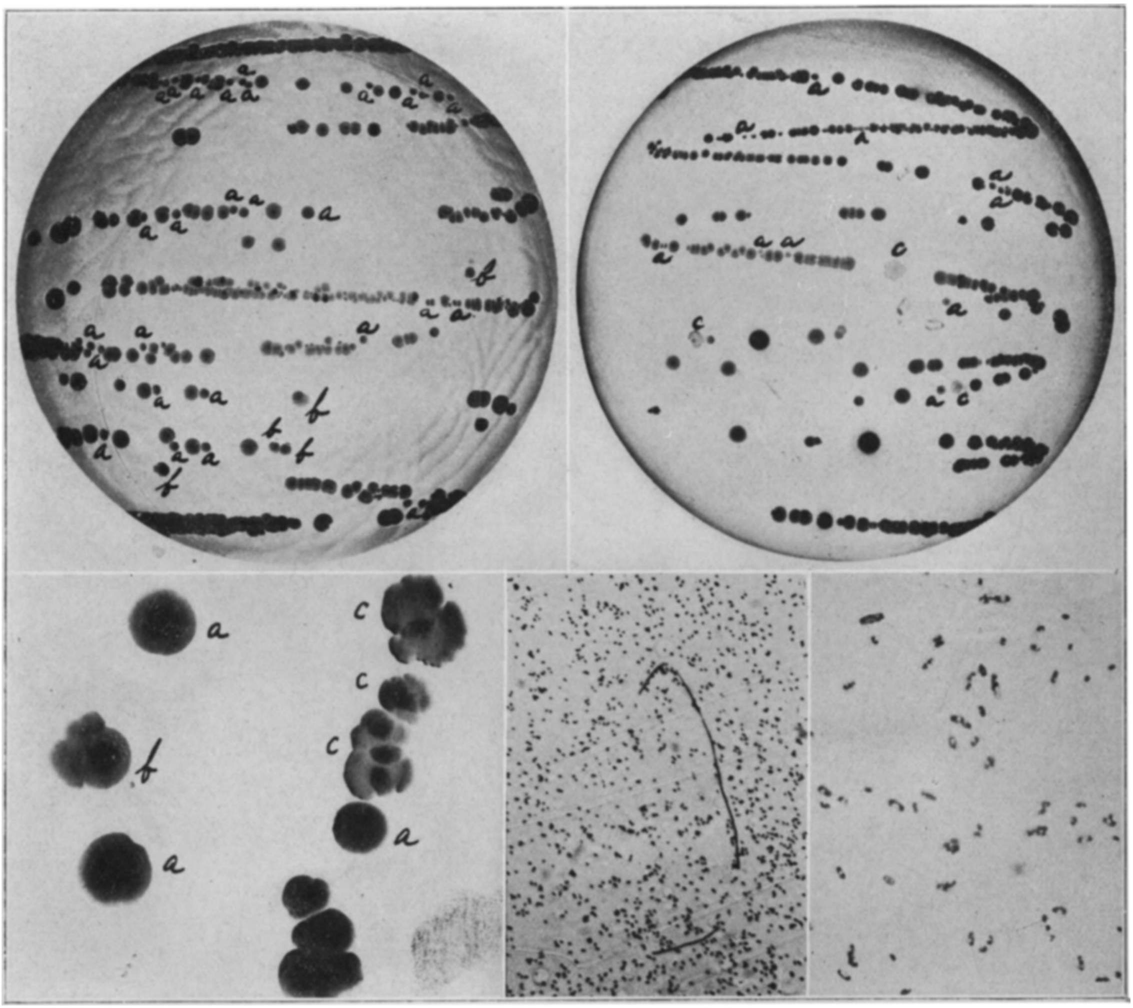
Various types of bacilli may be the causative agents of dysentery and dysenteric affections in children. While as a rule the dysentery bacilli are isolated, not infrequently the other kinds of bacilli are present. On the basis of these investigations it seems that at least one fourth of the cases are traceable to organisms not of the true dysentery type. Of the organisms producing dysenteric symptoms, aside from the true dysentery bacillus, in the majority of cases the paradysentery bacillus now described is found.

The paradysentery bacilli are small rods having no motion of their own, and forming acids by the fermentation of glucose but no gases. Two or three weeks after cultivation, milk begins to coagulate from the bottom up, and coagulation is completed with a few days. Older strains will coagulate milk even sooner. In addition to the characteristic round colonies, our paradysentery bacilli form also irregular colonies. The paradysentery group may be divided into two types, A and B, according to the carbohydrate decomposition produced. The organisms are infectious and pathogenic in character, and produce slight diphtheric inflammation on the intestinal wall.

The disease caused by paradysentery bacilli group should be called paradysentery.

In addition to the bacteria mentioned, the symptoms of dysentery may occasionally be produced also by paratyphoid or similar organisms. One group consists of rodlike organisms possessing feeble motility (?) which form acid and gas from mannite and dextrose, but do not affect saccharose, maltose, dextrin and lactose. These organisms, when attacking man, produce slight dysentric or typhoid symptoms. The organism is called "Paratyphoid X bacillus."

Plate 1



Figs. 1 and 2.—Colonies of paradysentery bacilli, isolated from the feces. Plain agar plate, natural size; a, round colonies; b, lobulated colonies; c, irregular colonies. Those not marked are colon bacilli.

Fig. 3.—Irregular colonies developing from a pure culture of the paradysentery bacillus. The changes in the shape of the colony do not indicate any change in the biologic properties of the organism.

Fig. 4.—Long chains of paradysentery bacilli, a feature of the organism which distinguishes it from the organisms of the dysentery group.

Fig. 5.—Bipolar staining of paradysentery bacilli; Ziehl's solution.